Application No.: 09/645,456
Applicant: Fu et al.
NOVEL GERMINAL CENTER KINASE CELL CYC
Sheet 1 of 35

				1	/ 35				
1 MASDSPARSLDEIDLSALRDPAGIFELVEIVGNGTYGQVYKGRHVKTGQLAAIKVMDVTGDEEEETKQEINMLKKYSHHR 1 MANDSPAKSLVDIDLSSLRDPAGIFELVEVVGNGTYGQVYKGRHVKT-VTAAIKVMDVTEDEEEETTLEINMLKKYSHHR	81 NIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSMTDLİKNTKGNTLKERWIAYICREILRGLSHLHQHKVIHRDIKGQNVL 80 NIATYYGAFIKKSPPGHDDQLWLVMEFCGAGSİTDLMKNTKGNTLKERMIAYISREILRGLAHLHIHEVIHRDIKGQNVL	161 LTENAEVKLVDFGVSAQLDRTVGRRNTFIGTPYWMÆPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR 160 LTENAEVKLVDFGVSAQLDRTVGRRNTFIGTPYWMAPEVIACDENPDATYDYRSDLWSCGITAIEMAEGGPPLCDMHPMR	241 ALFLIPRNPAPRLKSKKWSKKFOSFIESCLVKNHSORPATEQLMKHPFIRDOPNEROVRIQLKDHIDRTKKKRGEKDETE 240 ALFLIPRNPPPRLKSKKWSKKFFSFIEGCLVKNYMORPSTEQLLKHPFIRDOPNEROVRIQLKDHIDRTRKKRGEKDETE	321 YEYSGSEEEEENDSGEPSSIÜNÜPGESTLRRDFLRLQLANKERSEALRRQQLEOOOREMEEHKRQLLAERQKRIE 320 YEYSGSEEEEEEVPEQEGEPSSIVNVPGESTLRRDFLRLQQENKERSEALRRQQLLOEQQLREGEEYKRQLLAERQKRIE	397 EQKEQRRRLEEQQRREKELRKOQEREQRR	460 ILQQQLLHEQAHLLEYXARXQLEEQRQAERLQRQLXQERDYLVSLQHQRQEQRPVEKKPLYHYKEGMSPSEKPAWAKEVEE 480 ILQQQLLQEQAMLLHDHRRPPHAQQ-QPPPPQQQDRXSKPSYHAPEPKP-KPAD	540 RSRLNRQSSPAMPHKVANRISDPNIPPRSESFSISGVQPARTPPMLRPVDPQIPHLVAVKSQGPALTASQSVHEQPTKGL 532 RAREVQWSHLASLKNNVSPVSRSHSFSDPSPKFAHHHLRSQDPCPPSR	620 SGFQEALNVTSHRVEMPRQNSDPTSENPPLPTRIEKFDRSSWLRQEED-IPPKVPQRTTSISPALARKNSPGMGSALGPR 584 SQSSDSKSE-VPEPTQKAWSRSDEVPPRVPVRTTSRSPVLSRRDFROSPUGGQQNS	699 LGSQPIRASNPDLRRTEPLLESPLORTSSGSSSISSTPSSQPSSQGGSQPGSQAGSSERTRVRANSKSEGSPVLPHEPAK 640 QAGQRNSTSSLEPRLLWERVEKLIVPRPGSGSSSGSSNSGSQPGSHPGSQSGSRFRVRSSSKSEGSPSPRQESAA
TNIK NIK	TNIK NIK	TNIK	TNIK NIK	TNIK	TNIK	TNIK NIK	TNIK NIK	TNIK NIK	TNIK

F/G._ 1/

Application No.: 09/645,456
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Sheet 2 of 35

2/35 EDEGVYVNTYGRITKDVVLQWGEMPTSVAYTHSNQIMGWGEKAIEIRSVETGHLDGVFMHKRAQRLKFLCERNDKVFFAS VLVTISGKKNKLRVYYLSWLRNRILHNDPEVEKKQGWITVGDLEGGIHYKVVKYERIKFLVIALKNAVERYRK edegvyvntygritkdvvlqwgemptsvay irsnomgegeraieirsvetghldgvfmhkragrikflggrndkvffas VLVTISGKK|DKLRVYYLSWLRN|K|ILHNDPEVEKKQGW|ПТVGDLEGC|VHYKVVKYERIKFLVIALKSS|VE|K|YAWAPKPYHK FMAFKSFROLQHKPLLVDLTVEEGQRLKVTFGSHTGFHVTDVDSGNSYDIYTPSHIQGNTTPHAIMILPKTDGMEMLVCY FMAFKSFIGED LIKPLLVDLTVEEGQRLKVINGSCAGFHANDVDSGSVYDIYDPMHIQCSIKPHALIILPNTDGMEHLVCY VRSGGSSQVYFMTLGRTSLLSW VRSGGSSQVFFMTLNRNSMMNW 1339 1099 972 1179 1052 1259 1132 1212 TNIK TNIK TNIK TNIK NIK NIK NIK NIK

DIPRLIPTGAPGSNEQYNVGMYGTHGLETSHADSFSGSISREGTLMTRETSGEKKRSGHSDSNGFAGHINLPDLVQQSHS EDTRAASSPNLSNGETESVKTMIVHDDVESEP---AMTPSKEGTLIVRQTQSASS---------TLQKHK

VKPEESKOTTRPSRPASYKKALIDEDLTALAKELREUR I BETNRPMKKVTDYSSSSEESESSEEDGESETHDGTVAVS

779716

TNIK

NIK

KRPDDKKEVFR-----SLKPAGEVDLTALAKELRAW---EDVRPFRKVTDYSSSSEESGTTDEEEEDVEOEGADDSTSGP

PAGTPTEGLGRVSTHSQEMDSGTEYGMGSSTRASFTPFWPPRWYQTSPTDEDEESSAAALFTSELLRQEQAKLNEAR

---SSSSFTPFIDPRITQISPSS--

KIIS VVNVNPTNIRPHSDTPEIRKYKKRFNSEILCAALWGVNLLVGTENGLMLLDRSGOGKVYNL INRRRFQQMDVLEGLN KGSVVNVNPTNTRPQSDTPEIRKYKKRFNSEILCAALWGVNLLVGTESGIMLLDRSGQGKVYPLTSRRFQQMDVLEGIN

1019

TNIK

892

NIK

939

TNIK

846

NIK

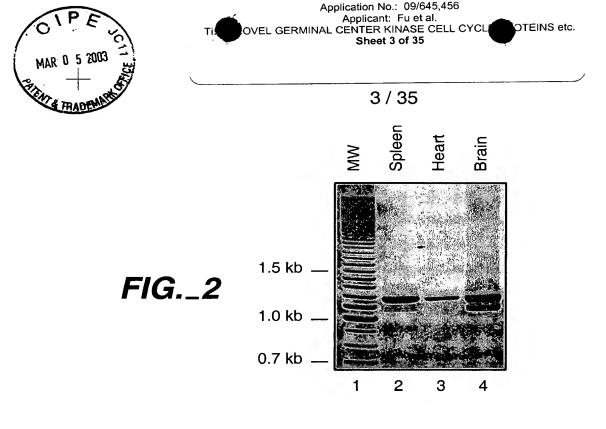
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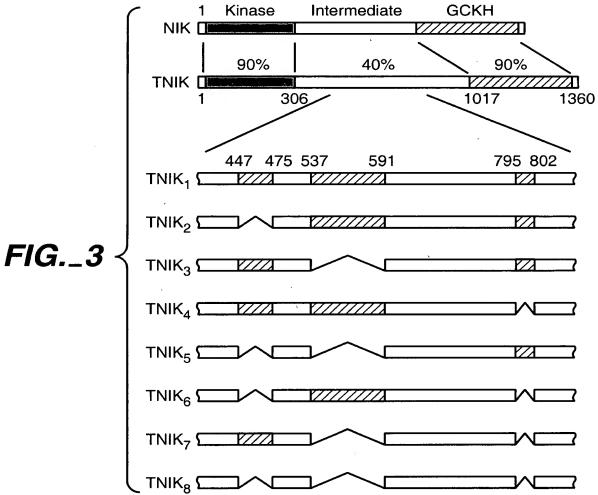
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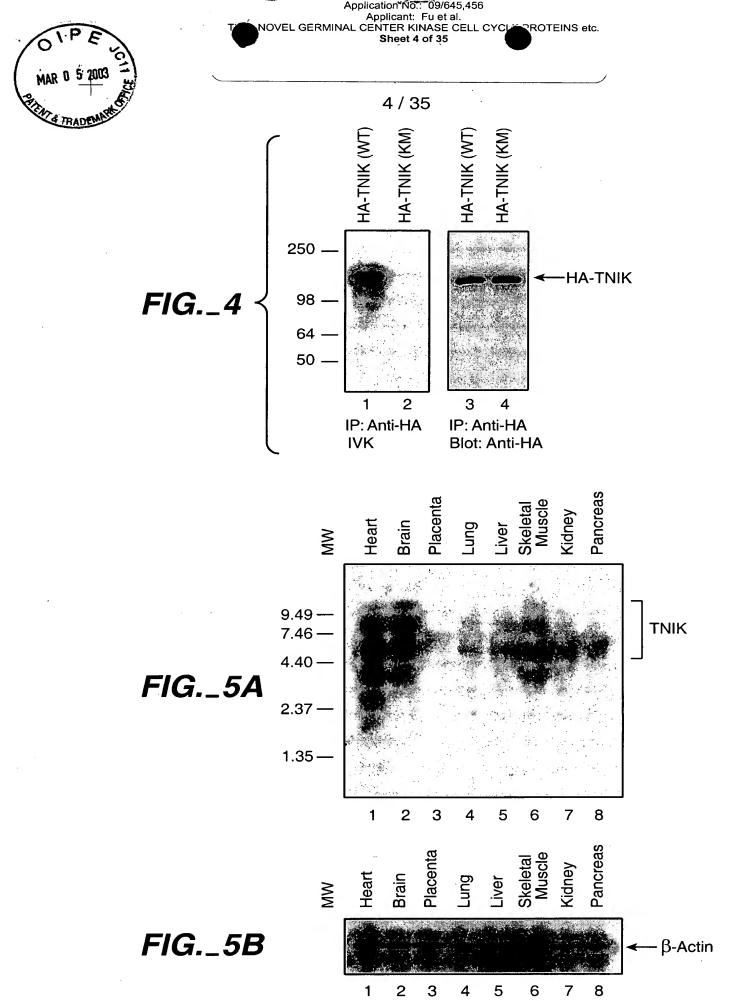
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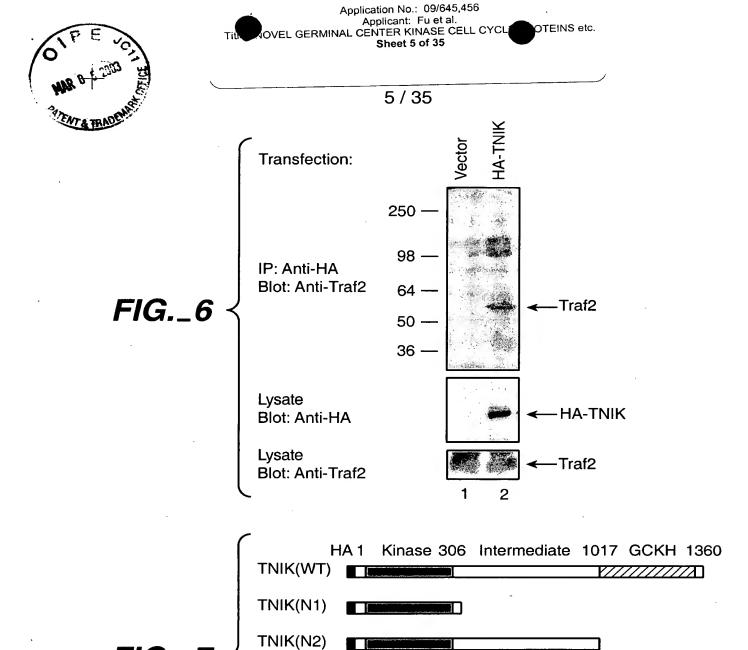
--GTTVTSVVGFSCDGLRPEAIRQDPTR

FIG._ 1B









TNIK(C1)

TNIK(C2)

TNIK(M)



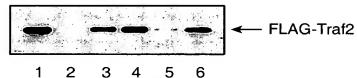
HA-TNIK Mutants

Transfection:

WT N1 N2 C1 C2 M

FIG._8A

IP: Anti-HA Blot: Anti-FLAG



HA-TNIK Mutants

Transfection:

WT N1 N2 C1 C2 M

FIG._8B

Lysate Blot: Anti-FLAG



- FLAG-Traf2

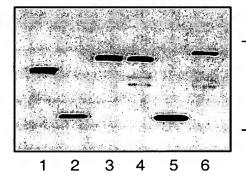
1 2 3 4 5 6

HA-TNIK Mutants

Transfection:

WT N1 N2 C1 C2 M

FIG._8C Lysate Blot: Anti-HA



HA-TNIK Mutants

FLAG 1 Ring 97 Zn Finger 272 Traf-N 355 Traf-C 501 Traf2 (WT)

Traf2 (1-272)

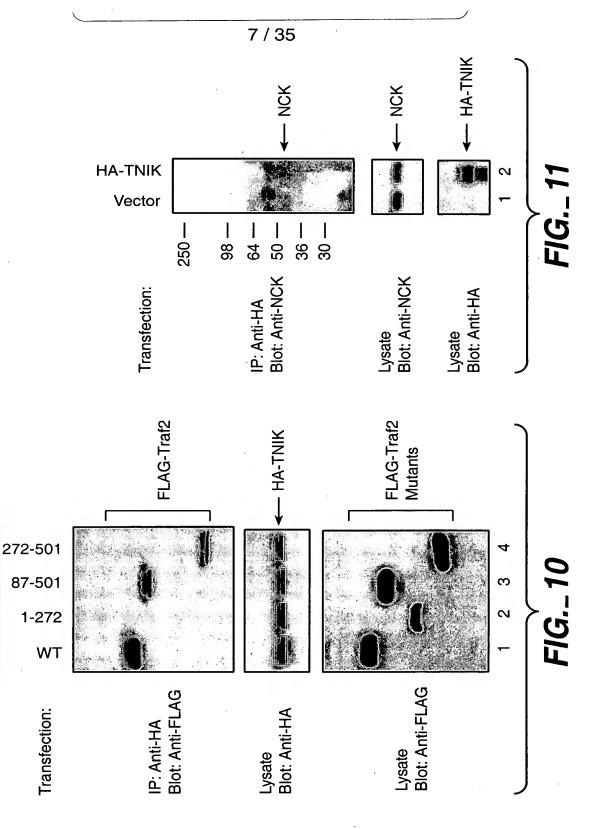
Traf2 (87-501)

Traf2 (272-501)

FIG._9

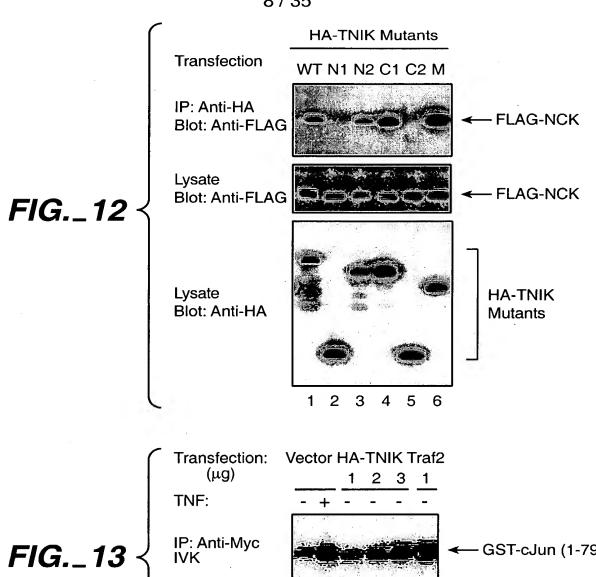


Traf2



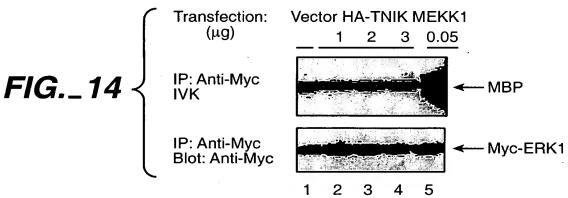


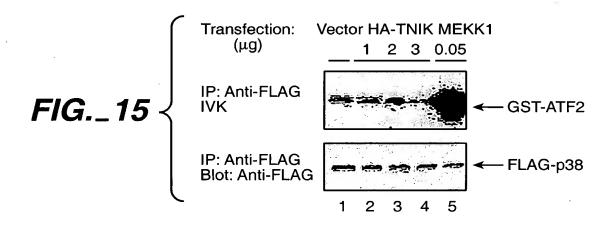
ROTEINS etc.

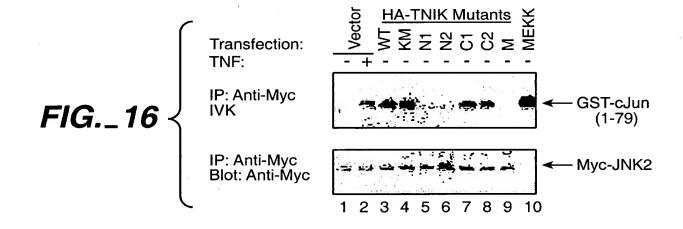


- GST-cJun (1-79) IP: Anti-Myc - MycJNK2 Blot: Anti-Myc 2 3 4 5 6











PROTEINS etc.

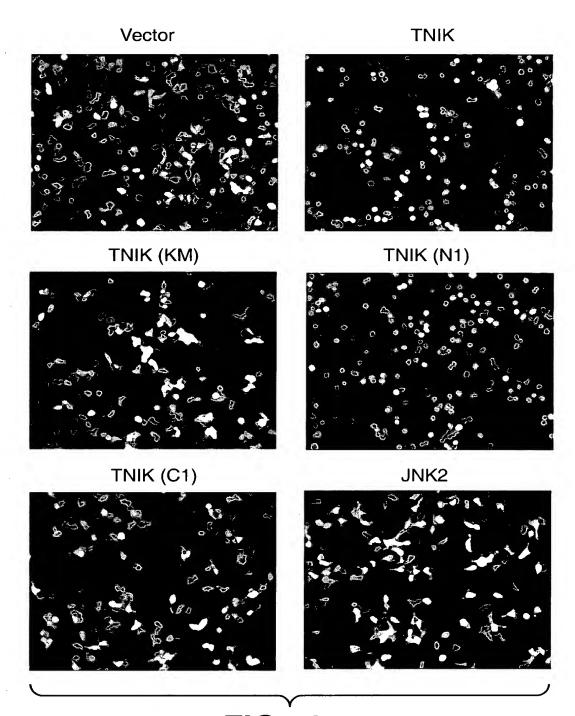
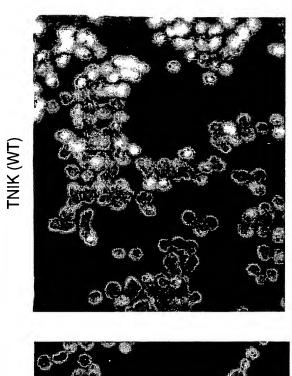
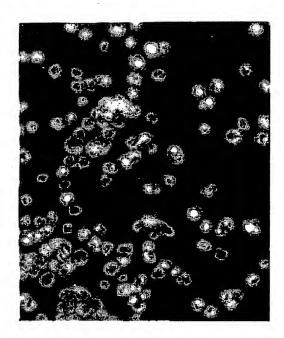
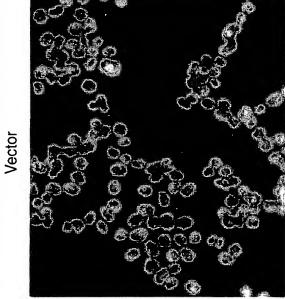


FIG._17









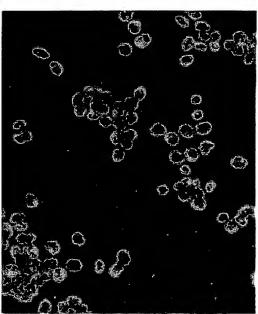
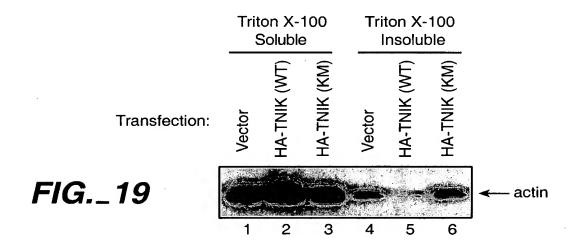


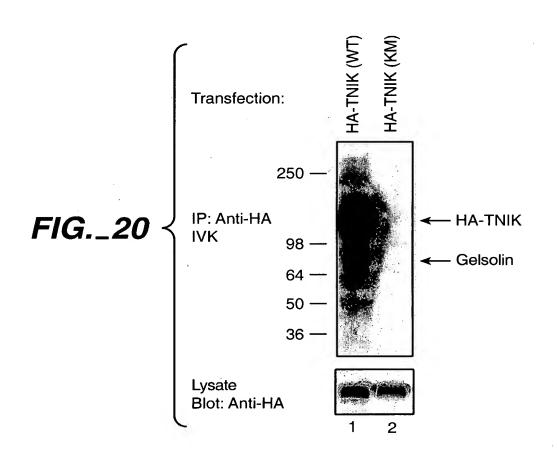
FIG._ 18

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TNIK (KM)





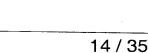




CTTTGGTTGGTGATGGAGTTTTGTGGTGCTGCTCTGTCACCGACCTGATCAAGAACACAAAAGGTAACACGTTG GCCTGTGATGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGGTCTTTGGGTATCACCGCCATTGAA **ATGGCAGAGGTGCTCCCCCTCTCTGTGACATGCACCCCATGAGGGCTCTCTTCCTCATCCCCCGGAATCCAGCG** AGTGAGGAAGAAGAGGAGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGGAGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATTCAAACAAGAAATTAACATGTTGAAGAAA TATTCTCATCACCGGAATATTGCTACATACTATGGTGCTTTTATCAAAAAGAACCCACCAGGCATGGATGACCAA CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGCGCATCGAGGAGCAGAAAGAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAGGAGCTGCGGAAGCAGCAGGAGGAGGAGCAGCGCCGG CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGGAGGAGCGTGCGGAGCATGAACAGGAATACATCAGGCGACAG GTTTCCCTTCAGCATCAGCGGCAGGAGCAGAGGCCTGTGGAGAAGAAGCCACTGTACCATTACAAAGAAGGAATG atggcgagcgactccccggctcgaagcctggatgaataaatctctcggctctgagggacctgcagggatctt GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT **LAAGAGGAGTGGATTGCATACATCTGCAGGGAAATCTTACGGGGGCTGAGTCACCTGCACCAGCATAAAGTGATT** CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT GCTCAGCTTGATCGAACAGTGGGCAGGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT CAGCGACCAGCAACAGAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT TTAGAGGAGGAGCAGACAGTTAGAGATCTTGCAGCAGCAGCTACTGCATGAACAAGCTCTACTTCTGGAATAT **AGTCCTAGTGAGAAGCCAGCATGGGCCAAGGAGGTAGAAGAACGGTCAAGGCTCAACCGGCAAAGTTCCCCTGCC** ATGCCTCACAAGGTTGCCAACAGGATATCTGACCCCAACCTGCCCCCAAGGTCGGAGTCCTTCAGCATTAGTGGA GTTCAGCCTGCTCGAACACCCCCCATGCTCAGACCAGTCGATCCCCAGATCCCACATCTGGTAGCTGTAAAATCC CAGGGACCTGCCTTGACCGCCTCCCAGTCAGTGCACGAGCACCACAAAGGGCCTCTCTGGGTTTCAGGAGGCT CTGAACGTGACCTCCCACCGCGTGGAGATGCCACGCCAGAACTCAGATCCCCACCTCGGAAAATCCTCCTCCCCC ACTCGCATTGAAAAGTTTGACCGAAGCTCTTGGTTACGACAGGAAGAGACATTCCACCAAAGGTGCCTCAAAGA

FIG._21A





ACAACTTCTATATCCCCAGCATTAGCCAGAAAGAATTCTCCTGGGAATGGTAGTGCTCTGGGACCCAGACTAGGA ICTCAACCCATCAGAGCAAGCAACCCTGATCTCCGGAGAACTGAGCCCATCTTGGAGAGCCCCTTGCAGAGGACC AGCAGTGGCAGTTCCTCCAGCTCCAGCACCCCTAGCTCCCAGCCCAGCTCCCAAGGAGGCTCCCAGCCTGGATCA CAAGCAGGATCCAGTGAACGCACCAGAGTTCGAGCCAACAGTAAGTCAGAAGGATCACCTGTGCTTCCCCATGAG GTGACTGATTACTCCTCCTCCAGTGAGGAGTCAGAAGTAGCGAGGAAGAGGAGGAAGATGGAGGAGAGAGCGAGACC CATGATGGGACAGTGGCTGTCAGCGACATACCCAGACTGATACCAACAGGAGCTCCAGGCAGCAACGAGCAGTAC **AATGTGGGAATGGTGGGGACGCATGGGCTGGAGACCTCTCATGCGGACAGTTTCAGCGGCAGTATTTCAAGAGAA** GGAACCTTGATGATTAGAGAGACGTCTGGAGAGAGAAGAGCGATCTGGCCACAGAGGCAATGGCTTTGCTGGC CACATCAACCTCCCTGACCTGGTGCAGAGCCATTCTCCAGCTGGAACCCCGACTGAGGGACTGGGGCGCGTC TCAACCCATTCCCAGGAGATGGACTCTGGGACTGAATATGGCATGGGGAGCAGCACCAAAGCCTCCTTCACCCCC **AACCCAACCAACATTCGGCCTCATAGCGACACACCAGAAATCAGAAATACAAGAAACGATTCAACTCAGAAATA** CTTTGTGCAGCTCTGTGGGGGTGTAAACCTTCTGGTGGGGACTGAAAATGGCCTGATGCTTTTGGACCGAAGTGGG TATCATAAATTCATGGCATTTAAGTCTTTTGCAGATCTCCAGCACAAGCCTCTGCTAGTTGATCTCACGGTAGAA TTTGTGGACCCCAGAGTATACCAGACGTCTCCCACTGATGAAGATGAAGAGGATGAGGAATCATCAGCCGCAGCT GTGACAATTTCAGGAAAGAAGAATAAGCTACGAGTTTACTATCTTTCATGGTTAAGAAACAGAATACTACATAAT **AAATATGAAAGGATCAAATTTTTGGTGATTGCCTTAAAGAATGCTGTGGAAATATATGCTTGGGCTCCTAAACCG** GACCCAGAAGTAGAAAAAAAAAAGGCTGGATCACTGTTGGGGACTTGGAAGGCTGTATACATTATAAAGTTGTT GAAGGTCAAAGATTAAAGGTTATTTTGGTTCACACAGTTTCCATGTAATTGATGTTGATTCAGGAAACTCT TATGATATCTACATACCATCTCATATTCAGGGCAATATCACTCCTCATGCTATTGTCATCTTGCCTAAAACAGAT TTTCTATGTGAAAAAAAAAAAGGTATTTTTGCATCCGTGCGATCTGGAGGAAGTAGCCAAGTGTTTTTCATG **ACCCTCAACAGAAATTCCATGATGAACTGGTAA**



ATGGCGAGCGACTCCCCGGCTCGAAGCCTGGATGAATAGATCTCTCGGCTCTGAGGGACCCTGCAGGGATCTTT GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATCAAACAAGAAATTAACATGTTGAAGAAA IATTCTCATCACCGGAATATTGCTACATACTATGGTGCTTTTATCAAAAAGAACCCACCAGGCATGGATGACCAA CTTTGGTTGGTGATGGAGTTTTGTGGTGCTGGCTCTGTCACCGACCTGATCAAGAACACAAAAAGGTAACACGTTG GCCTGTGAGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGTCTTTGGGTATCACCGCCATTGAA **ATGGCAGAGGAGGTGCTCCCCCTCTGTGACATGCACCCCATGAGAGCTCTTCCTCATCCCCCCGGAATCCAGCG** CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC AGTGAGGAAGAGAGGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGAGGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG TCCCACCGCGTGGAGATGCCACGCCAGAACTCAGATCCCACCTCGGAAAATCCTCCTCTCCCCACTCGCATTGAA <u> paagaggagtggattgcatacatctgcagggaaatcttacgggggctgagtcacctgcaccagcataaagtgatt</u> CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT GCTCAGCTTGATCGAACAGTGGGCAGGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGCGCATCGAGGAGCAAAAAGAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAAGGAGCTGCGGAAGCAGCAGCAGGAGAGAGGAGAGCAGCGCCGG CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGGAGGAGGCGTGCGGAGCATGAACAGGAATATAAGCGCAAACAA CATCAGCGGCAGGAGCAGAGGCCTGTGGAGAAGAAGCCACTGTACCATTACAAAGAAGGAATGAGTCCTAGTGAG **AAGCCAGCATGGGCCAAGGAGGTAGAAGAACGGTCAAGGCTCAACCGGCAAAGTTCCCCTGCCATGCCTCACAAG** CGAACACCCCCCATGCTCAGACCAGTCGATCCCCAGATCCCACATCTGGTAGCTGTAAAATCCCAGGGACCTGCC TTGACCGCCTCCCAGTCAGTGCACGAGCAGCCCCACAAAGGGCCTCTCTGGGTTTCAGGAGGCTCTGAACGTGACC **AAGTITGACCGAAGCTCTTGGTTACGACAGGAAGAGACATTCCACCAAAGGTGCCTCAAAGAACAACTTCTATA** TCCCCAGCATTAGCCAGAAAGAATTCTCCTGGGAATGGTAGTGCTCTGGGACCCAGACTAGGATCTCAACCCATC CAGCGACCAGCAACAGAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT STTGCCAACAGGATATCTGACCCCAACCTGCCCCCAAGGTCGGAGTCCTTCAGCATTAGTGGAGTTCAGCCTGCT AGAGCAAGCAACCCTGATCTCCGGAGAACTGAGCCCCATCTTGGAGAGCCCCTTGCAGAGGACCAGCAGTGGCAGT

FIG._22A



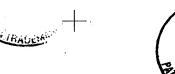
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FIG._22B

CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGAGGGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAGAAGGAGCTGCGGAAGCAGCAGCAGGAGAGGAGCAGCAGCCGG CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGGAGGCGTGCGGAGCATGAACAGGAATACATCAGGCGACAG GTTTCCCTTCAGCATCAGCGGCAGGAGCAGAGGCCTGTGGAGAAGAAGAAGCCACTGTACCATTACAAAGAAGGAATG AGTCCTAGTGAGAAGCCAGCATGGGCCAAGGAGATCCCACATCTGGTAGCTGTAAAATCCCAGGGACCTGCCTTG **ACCGCCTCCCAGTCAGTGCACGAGCAGCCCACAAAGGGCCTCTCTGGGTTTCAGGAGGCTCTGAACGTGACCTCC** CACCGCGTGGAGATGCCACGCCAGAACTCAGATCCCACCTCGGAAAATCCTCCTCTCCCCACTCGCATTGAAAA TTTGACCGAAGCTCTTGGTTACGACAGGAAGAAGACATTCCACCAAAGGTGCCTCAAAGAACAACTTCTATATCC CCAGCATTAGCCAGAAAGAATTCTCCTGGGAATGGTAGTGCTCTGGGACCCAGACTAGGATCTCAACCCATCAGA GCAAGCAACCCTGATCTCCGGAGAACTGAGCCCATCTTGGAGAGCCCCTTGCAGAGGACCAGCAGTGGCAGTTCC GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATCAAACAAGAAATTAACATGTTGAAGAAA CTTTGGTTGGTGATGGAGTTTTGTGGTGCTGCTCTGTCACCGACCTGATCAAGAACACAAAAGGTAACACGTTG CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT GCCTGTGAGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGTCTTTGGGTATCACCGCCATTGAA ATGGCAGAAGGTGCTCCCCCTCTGTGACATGCACCCCATGAGAGCTCTTCCTCATCCCCCCGGAATCCAGCG CAGCGACCAGCAACAGAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT AGTGAGGAAGAGAGGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGCGCATCGAGGAGCAGAAAAAG TTAGAGGAGGAGCAGACAGTTAGAGATCTTGCAGCAGCAGCTACTGCATGAACAAGCTCTACTTCTGGAATAT aagcgcaaacaattggaagaacagagacaagcagaaagctgcagagggcagctaaagcaaggaaaaagagctactta <u>AAAGAGGAGTGGATTGCATACATCTGCAGGGAAATCTTACGGGGGCTGAGTCACCTGCACCAGCATAAAGTGATT</u> GCTCAGCTTGATCGAACAGTGGGCAGGAAGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT **GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT**

FIG._23A





ATGGCGAGCGACTCCCCGGCTCGAAGCCTGGATGAATAGATCTCTCGGCTCTGAGGGACCCTGCAGGGATCTTT



GCTGTCAGCGACATACCCAGACTGATACCAACAGGAGCTCCAGGCAGCAACGAGCAGTACAATGTGGGAATGGTG GACCTGGTGCAGCAGAGCCATTCTCCAGCTGGAACCCCGACTGAGGGACTGGGGCGCGCGTCTCAACCCATTCCCAG AAGAAACAAGGCTGGATCACTGTTGGGGACTTGGAAGGCTGTATACATTATAAAGTTGTTAAATATGAAAGGATC AAATTTTTGGTGATTGCCTTAAAGAATGCTGTGGAAATATATGCTTGGGCTCCTAAACCGTATCATAAATTCATG GCATTTAAGTCTTTTGCAGATCTCCAGCACAAGCCTCTGCTAGTTGATCTCACGGTAGAAGAAGGTCAAAGATTA AAGGTTATTTTGGTTCACACACTGGTTTCCATGTAATTGATGTTGATTCAGGAAACTCTTATGATATCTACATA GTTTGCTATGAGGATGAGGGGGTGTATGTAACACCTATGGCCGGATAACTAAGGATGTGGTGCTCCAATGGGGA SAAATGCCCACGTCTGTGGCCTACATTCATTCCAATCAGATAATGGGCTGGGGCGAGAAAGCTATTGAGATCCGG TCAGTGGAAACAGGACATTTGGATGGAGTATTTATGCATAAGCGAGCTCAAAGGTTAAAGTTTCTATGTGAAAGA GAACGCACCAGAGTTCGAGCCAACAGTAAGTCAGAAGGATCACCTGTGCTTCCCCATGAGCCTGCCAAGGTGAAA GGGACGCATGGGCTGGAGACCTCTCATGCGGACAGTTTCAGCGGCAGTATTTCAAGAGAAGGAACCTTGATGATT GAGATGGACTCTGGGACTGAATATGGCATGGGGAGCAGCACCAAAAGCCTCCTTCACCCCCTTTGTGGACCCCAGA GTATACCAGACGTCTCCCACTGATGAAGATGAAGAGGATGAGGAATCATCAGCCGCAGCTCTGTTTACTAGCGAA CGGCCTCATAGCGACACACACAGAAATCAGAAATACAAGAAACGATTCAACTCAGAAATACTTGTGCAGCTCTG TGGGGTGTAAACCTTCTGGTGGGGACTGAAAATGGCCTGATGCTTTTGGACCGAAGTGGGCAAGGCAAAGTCTAT <u> AATCTGATCAACCGGAGGCGATTTCAGCAGATGGATGTGCTAGAGGGACTGAATGTCCTTGTGACAATTTCAGGA</u> **AAGAAGAATAAGCTACGAGTTTACTATCTTTCATGGTTAAGAAACAGAATACTACATAATGACCCAGAAGTAGAA AATGATAAGGTATTTTTTGCATCCGTGCGATCTGGAGGAAGTAGCCAAGTGTTTTTCATGACCCTCAACAGAAAT** TCCAGCTCCAGCACCCCTAGCTCCCAGCCCAGCTCCCAAGGAGGCTCCCAGCCTGGATCACAAGCAGGATCAGA **AGAGAGACGTCTGGAGAGAAGAAGCGATCTGGCCACAGTGACAGCAATGGCTTTGCTGGCCACATCAACCTCCCT** CCATCTCATATTCAGGGCAATATCACTCCTCATGCTATTGTCATCTTGCCTAAAACAGATGGAATGGAAATGCTT *ICCATGATGAACTGGTAA*

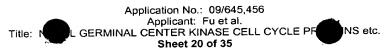
FIG._23B

TEINS etc.

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ATGGCGAGCGACTCCCCGGCTCGAAGCCTGGATGAATAGATCTCTCGGCTCTGAGGGACCCTGCAGGGATCTTT GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATCAAACAAGAAATTAACATGTTGAAGAAA CTTTGGTTGGTGATGGAGTTTTGTGGTGCTGGCTCTGTCACCGACCTGATCAAGAACACAAAAAGGTAACACGTTG CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC <u> AAAGAGGAGTGGATTGCATACATCTGCAGGGAAATCTTACGGGGGCTGAGTCACCTGCACCAGCATAAAGTGATT</u> CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT GCTCAGCTTGATCGAACAGTGGGCAGGAGGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT GCCTGTGATGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGGTCTTTGGGTATCACCGCCATŢGAA ATGGCAGAGGTGCTCCCCTCTCTGTGACATGCACCCCATGAGGCTCTCTTCCTCATCCCCCGGAATCCAGCG CAGCGACCAGCAACAGAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT AGTGAGGAAGAAGAGGAGGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGGAGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGCGCATCGAGGAGCAGAAAGAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAGAAGGAGCTGCGGAAGCAGCAGCAGGAGGAGGAGCAGCCGG CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGAGGAGGCGTGCGGAGCATGAACAGGAATACATCAGGCGACAG TTAGAGGAGGAGCAGAGACAGTTAGAGATCTTGCAGCAGCAGCTACTGCATGAACAAGCTCTACTTCTGGAATAT GTTTCCCTTCAGCATCAGCGGCAGGAGCAGGCCTGTGGAGAAGAAGAAGCCACTGTACCATTACAAAGAAGGAATG AGTCCTAGTGAGAAGCCAGCATGGGCCAAGGAGGTAGAAGAACGGTCAAGGCTCAACCGGCAAAGTTCCCCTGCC ATGCCTCACAAGGTTGCCAACAGGATATCTGACCCCAACCTGCCCCCAAGGTCGGAGTCCTTCAGCATTAGTGGA GTTCAGCCTGCTCGAACACCCCCCCATGCTCAGACCAGTCGATCCCCAGATCCCACATCTGGTAGCTGTAAAATCC CAGGGACCTGCCTTGACCGCCTCCCAGTCAGTGCACGAGCAGCCCCACAAAGGGCCTCTCTGGGTTTTCAGGAGGCT CTGAACGTGACCTCCCACCGCGTGGAGATGCCACGCCAGAACTCAGATCCCACCTCGGAAAATCCTCCTCCTCCCC ACTCGCATTGAAAAGTTTGACCGAAGCTCTTGGTTACGACAGGAAGAAGACATTCCACCAAAGGTGCCTCAAAGA ACAACTTCTATATCCCCAGCATTAGCCAGAAAGAATTCTCCTGGGAATGGTAGTGCTCTGGGACCCAGACTAGGA





ICTCAACCCATCAGAGCAAGCAACCCTGATCTCCGGAGAACTGAGCCCATCTTGGAGAGCCCCTTGCAGAGGACC CAAGCAGGATCCAGTGAACGCACCAGAGTTCGAGCCAACAGTAAGTCAGAAGGATCACCTGTGCTTCCCCATGAG AGCAGTGGCAGTTCCTCCAGCTCCAGCACCCCTAGCTCCCAGCCCCAGCTCCCAAGGAGGCTCCCAGCCTGGATCA CCTGCCAAGGTGAAACCAGAAGAATCCAGGGACATTACCCGGCCCAGTCGACCAGCTGATCTGACGGCATTAGCC AAAGAACTAAGAGAACTCCGGATTGAAGAAACAACCGCCCAATGAAGAAGGTGACTGATTACTCCTCCTCCAGT GAGGAGTCAGAAAGTAGCGAGGAAGAGGAGGAAGATGGAGAGGGGAGAGCCCATGATGGGACAGTGGCTGTCAGC GACATACCCAGACTGATACCAACAGGAGCTCCAGGCAGCAACGAGCAGTACAATGTGGGGAATGGTGGGGGACGCAT GGGCTGGAGACCTCTCATGCGGACAGTTTCAGCGGCAGTATTTCAAGAGAAGGAACCTTGATGATTAGAGAGCG TCTGGAGAGAAGAAGCGATCTGGCCACAGTGACAGCAATGGCTTTGCTGGCCACATCAACCTCCCTGACCTGGTG CAGCAGAGCCATTCTCCAGCTGGAACCCCGACTGAGGGACTGGGGCGCGTCTCAACCCATTCCCAGGAGATGGAC TCTGGGACTGAATATGGCATGGGGAGCAGCACCAAAGCCTCCTTCACCCCCTTTGTGGACCCCAGAGTATACCAG **ACGTCTCCCACTGATGAAGATGAGGATGAGGAATCATCAGCCGCAGCTCTGTTTACTAGCGAACTTCTTAGG AGCGACACACCAGAAATCAGAAATACAAGAAACGATTCAACTCAGAAATACTTTGTGCAGCTCTGTGGGGTGTA** GGCTGGATCACTGTTGGGGACTTGGAAGGCTGTATACATTATAAAGTTGTTAAATATGAAAGGATCAAATTTTTG GTGATTGCCTTAAAGAATGCTGTGGAAATATATGCTTGGGCTCCTAAACCGTATCATAAATTCATGGCATTTAAG ACGTCTGTGGCCTACATTCATTCCAATCAGATAATGGGCTGGGGCGAGAAAGCTATTGAGATCCGGTCAGTGGAA **AACCTTCTGGTGGGGACTGAAAATGGCCTGATGCTTTTGGACCGAAGTGGGCAAGGCAAAGTCTATAATCTGATC** aaccggaggcgatttcagcagatggatgtgctagagggactgaatgtcttgtgacaatttcaggaaagaat TCTTTTGCAGATCTCCAGCACAAGCCTCTGCTAGTTGATCTCACGGTAGAAGAAGGTCAAAGATTAAAGGTTATT **TTTGGTTCACACACTGGTTTCCATGTAATTGATGTTGATTCAGGAAACTCTTATGATATCTACATACCATCTCAT** GAGGATGAGGGGGTGTATGTAAACACCTATGGCCGGATAACTAAGGATGTGGTGCTCCAATGGGGAGAAATGCCC GTATTTTTTGCATCCGTGCGATCTGGAGGAAGTAGCCAAGTGTTTTTCATGACCCTCAACAGAAATTCCATGATG ATTCAGGGCAATATCACTCCTCATGCTATTGTCATCTTGCCTAAAACAGATGGAATGGAAATGCTTGTTTGCTAT

FIG._24B



CTTTGGTTGGTGATGGAGTTTTGTGGTGCTCTGTCACCGACCTGATCAAGAACACAAAAGGTAACACGTTG atgecgagcgactccccggctcgaagcctggatgaatagatctctcggctctgaggaccctgcaggatctt GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATCAAACAAGAAATTAACATGTTGAAGAAA TATTCTCATCACCGGAATATTGCTACATACTATGGTGCTTTTTATCAAAAGAACCCACCAGGCATGGATGACCAA CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT GCTCAGCTTGATCGAACAGTGGGCAGGAGGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT GCCTGTGATGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGTTTTGGGTATCACCGCCATTGAA **ATGGCAGAAGGTGCTCCCCCTCTCTGTGACATGCACCCCCATGAGAGCTCTTCTTCCTCATCCCCGGAATCCAGCG** CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC AGTGAGGAAGAAGAGGAGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG AAGCCAGCATGGGCCAAGGAGATCCCACATCTGGTAGCTGTAAAATCCCAGGGA®CTGCCTTGACCGCCTCCCAG TCAGTGCACGAGCAGCCCACAAAGGGCCTCTCTGGGTTTCAGGAGGCTCTGAACGTGACCTCCCACCGCGTGGAG CAGCGACCAGCAACAGAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGAGGGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGCGCATCGAGGAGCAGAAAAAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAAGGAGCTGCGGAAGCAGCAGCAGGAGAGGAGCAGCCGG CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGGAGGCGTGCGGAGCATGAACAGGAATATAAGCGCAAACAA CATCAGCGGCAGGAGCAGAGGCCTGTGGAGAAGAAGCCACTGTACCATTACAAAGAAGGAATGAGTCCTAGTGAG **ATGCCACGCCAGAACTCAGATCCCACCTCGGAAATCCTCCTCCTCCCCACTCGCATTGAAAGTTTGACCGAAGC** TCTTGGTTACGACAGGAAGAAGAAGATTCCACCAAAGGTGCCTCAAAGAACAACTTCTATATCCCCCAGCATTAGCC GATCTCCGGAGAACTGAGCCCATCTTGGAGAGCCCCTTGCAGAGGACCAGCAGTGGCAGTTCCTCCAGCTCCAGC ACCCCTAGCTCCCAGCCCAGCTCCCAAGGAGGCTCCCAGCCTGGATCACAAGCAGGATCCAGTGAACGCACCAGA

FIG._25A



GTTCGAGCCAACAGTAAGTCAGAAGGATCACCTGTGCTTCCCCATGAGCCTGCCAAGGTGAAACCAGAAGAATCC AGGGACATTACCCGGCCCAGTCGACCAGCTAGCTACAAAAAGCTATAGATGAGGATCTGACGGCATTAGCCAAA GAACTAAGAGAACTCCGGATTGAAGAAACAAACCGCCCAATGAAGAAGGTGACTGATTACTCCTCCTCCAGTGAG GGAGAGAAGAAGCGATCTGGCCACAGTGACAGCAATGGCTTTGCTGGCCACATCAACCTCCCTGACCTGGTGCAG ATACCCAGACTGATACCAACAGGAGCTCCAGGCAGCACGAGCAGTACAATGTGGGAATGGTGGGGACGCATGGG CTGGAGACCTCTCATGCGGACAGTTTCAGCGGCAGTATTTCAAGAAGAAGGAACCTTGATGATTAGAGAGGACGTCT GGGACTGAATATGGCATGGGGAGCAGCACCAAAGCCTCCTTCACCCCCTTTGTGGACCCCCAGAGTATACCAGACG TCTCCCACTGATGAAGATGAAGATGAGGAATCATCAGCCGCAGCTCTGTTTACTAGCGAACTTCTTAGGCAA GACACACCAGAAATCAGAAATACAAGAAACGATTCAACTCAGAAATACTTTGTGCAGCTCTGTGGGGTGTAAAC CTTCTGGTGGGGACTGAAAATGGCCTGATGCTTTTGGACCGAAGTGGGCAAGGCAAAGTCTATAATCTGATCAAC CAGAGCCATTCTCCAGCTGGAACCCCGACTGAGGGACTGGGGCGCGTCTCAACCCATTCCCAGGAGATGGACTCT CGGAGGCGATTTCAGCAGATGGATGTGCTAGAGGGACTGAATGTCCTTGTGACAATTTCAGGAAAGAAGAATAAG TGGATCACTGTTGGGGACTTGGAAGGCTGTATACATTATAAAGTTGTTAAATATGAAAGGATCAAATTTTTGGTG ATTGCCTTAAAGAATGCTGTGGAAATATATGCTTGGGCTCCTAAACCGTATCATAAATTCATGGCATTTAAGTCT TTTGCAGATCTCCAGCACAAGCCTCTGCTAGTTGATCTCACGGTAGAAGAAGGTCAAAGATTAAAGGTTATTTTT GGTTCACACACTGGTTTCCATGTAATTGATGTTGATTCAGGAAACTCTTATGATATCTACATACCATCTCATATT CAGGGCAATATCACTCCTCATGCTATTGTCATCTTGCCTAAAACAGATGGAATGGAAATGCTTGTTTGCTATGAG GATGAGGGGGTGTATGTAAACACCTATGGCCGGATAACTAAGGATGTGGGTGCTCCAATGGGGAGAAATGCCCACG TCTGTGGCCTACATTCATTCCAATCAGATAATGGGCTGGGGGGAAAAGCTATTGAGATCCGGTCAGTGGAAACA ITTTTTGCATCCGTGCGATCTGGAGGAAGTAGCCAAGTGTTTTTCATGACCCTCAACAGAAATTCCATGATGAAC

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CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC AGTGAGGAAGAGAGAGGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG ATGGCGAGCGACTCCCCGGCTCGAAGCCTGGATGAATAGATCTCTCGGCTCTGAGGGACCCTGCAGGGATCTTT GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATCAAACAAGAAATTAACATGTTGAAGAAA CTTTGGTTGGTGATGGAGTTTTGTGGTGCTGCTCTGTCACCGACCTGATCAAGAACACAAAAGGTAACACGTTG <u> PAAGAGGAGTGGATTGCATACATCTGCAGGGAAATCTTACGGGGGCTGAGTCACCTGCACCAGCATAAAGTGATT</u> CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT GCTCAGCTTGATCGAACAGTGGGCAGGAGGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT GCCTGTGATGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGTCTTTGGGTATCACCGCCATTGAA **ATGGCAGAAGGTGCTCCCCCTCTGTGACATGCACCCCATGAGAGCTCTTCCTCATCCCCCGGAATCCAGCG** CAGCGACCAGCAACAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGGAGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGAGCGCATCGAGGAGCAGAAAGAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAAGGAGCTGCGGAAGCAGCAGCAGGAGAGGGAGCAGCCCGG CATCAGCGGCAGGAGCAGAGGCCTGTGGAGAAGAAGCCACTGTACCATTACAAAGAAGGAATGAGTCCTAGTGAG AAGCCAGCATGGGCCAAGGAGGTAGAAGAACGGTCAAGGCTCAACCGGCAAAGTTCCCCTGCCATGCCTCACAAG CGAACACCCCCCATGCTCAGACCAGTCGATCCCCAGATCCCACATCTGGTAGCTGTAAAATCCCAGGGACCTGCC receaececetecateceaeceaeceaegaaeteceaecaecaecaeaaaatectecteceeaetegaa AAGTTTGACCGAAGCTCTTGGTTACGACAGGAAGAGACATTCCACCAAAGGTGCCTCAAAGAACAACTTCTATA **ICCCCAGCATTAGCCAGAAGAATTCTCCTGGGAATGGTAGTGCTCTGGGACCCAGACTAGGATCTCAACCCATC** CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGGAGGCGTGCGGAGCATGAACAGGAATATAAGCGCAAACAA GTTGCCAACAGGATATCTGACCCCAACCTGCCCCCAAGGTCGGAGTCCTTCAGCATTAGTGGAGTTCAGCCTGCT

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AGTGAACGCACCAGAGTTCGAGCCAACAGTAAGTCAGAAGGATCACCTGTGCTTCCCCATGAGCCTGCCAAGGTG AAACCAGAAGAATCCAGGGACATTACCCGGCCCAGTCGACCAGCTGATCTGACGGCATTAGCCAAAGAACTAAGA GAACTCCGGATTGAAGAAACAAACCGCCCAATGAAGAAGGTGACTGATTACTCCTCCTCCAGTGAGGAGTCAGAA TCTCATGCGGACAGTTTCAGCGGCAGTATTTCAAGAGAAGGAACCTTGATGATTAGAGAGACGTCTGGAGAGAAG TCCTCCAGCTCCAGCACCCCTAGCTCCCAGCCCAGCTCCCAAGGAGGCTCCCAGCCTGGATCACAAGCAGGATCC AGTAGCGAGGAAGAGGAGGAGATGGAGAGAGCGAGACCCATGATGGGACAGTGGCTGTCAGCGACATACCCAGA CTGATACCAACAGGAGCTCCAGGCAGCAACGAGCAGTACAATGTGGGAATGGTGGGGACGCATGGGCTGGAGACC <u> AAGCGATCTGGCCACAGTGACAGCAATGGCTTTGCTGGCCACATCAACCTCCTGACCTGGTGCAGCAGAGCCAT</u> TCTCCAGCTGGAACCCCGACTGAGGGACTGGGGCGCGTCTCAACCCATTCCCAGGAGATGGACTCTGGGACTGAA TATGGCATGGGGAGCAGCACCAAAGCCTCCTTCACCCCTTTGTGGACCCCAGAGTATACCAGACGTCTCCCAC GATGAAGATGAAGAGGAATCATCACCGCCGCAGCTCTGTTTACTAGCGAACTTCTTAGGCAAGAACAGGCC GAAATCAGAAAATACAAGAAACGATTCAACTCAGAAATACTTTGTGCAGCTCTGTGGGGGTGTAAACCTTCTGGTG STTGGGGACTTGGAAGGCTGTATACATTATAAGTTGTTAAATATGAAAGGATCAAATTTTTGGTGATTGCCTTA CTCCAGCACAAGCCTCTGCTAGTTGATCTCACGGTAGAAGAAGGTCAAAGATTAAAGGTTATTTTTGGTTCACAC **ATCACTCCTCATGCTATTGTCATCTTGCCTAAAACAGATGGAATGGAAATGCTTGTTTGCTATGAGGATGAGGGG** GTGTATGTAAACACCTATGGCCGGATAACTAAGGATGTGGTGCTCCAATGGGGAGAAATGCCCACGTCTGTGGCC
 TACATTCATTCCAATCAGATAATGGGCTGGGCCGAGAAGCTATTGAGATCCGGTCAGTGGAAACAGGACATTTG
 GGGACTGAAAATGGCCTGATGCTTTTGGACCGAAGTGGGCAAGGCAAAGTCTATAATCTGATCAACCGGAGGCGA **AAGAATGCTGTGGAAATATATGCTTGGGCTCCTAAACCGTATCATAAATTCATGGCATTTAAGTCTTTTGCAGAT** ACTGGTTTCCATGTAATTGATGTTGATTCAGGAAACTCTTATGATATCTACATACCATCTCATATTCAGGGCAAT TTTCAGCAGATGGATGTGCTAGAGGGACTGAATGTCCTTGTGACAATTTCAGGAAAGAAGAATAAGCTACGAGTT **FCCGTGCGATCTGGAGGAAGTAGCCAAGTGTTTTTCATGACCCTCAACAGAAATTCCATGATGAACTGGTAA>**

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GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATCAAACAAGAAATTAACATGTTGAAGAAA FATTCTCATCACCGGAATATTGCTACATACTATGGTGCTTTTATCAAAAAGAACCCACCAGGCATGGATGACCAA CTTTGGTTGGTGATGGAGTTTTGTGGTGCTGTCTGTCACCGACCTGATCAAGAACACAAAAGGTAACACGTTG GCTCAGCTTGATCGAACAGTGGGCAGGAGGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT GCCTGTGATGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGTCTTTGGGTATCACCGCCATTGAA ATGGCAGAAGGTGCTCCCCCTCTGTGACATGCACCCCATGAGAGCTCTTCTTCCTCATCCCGGAATCCAGCG CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC CAGCGACCAGCAACAGAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT AGTGAGGAAGAAGAGAGGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGGAGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGCGCATCGAGGAGCAGAAAGAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAAGGAGCTGCGGAAGCAGCAGCAGGAGAGGGGAGCAGCCGG CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGGAGGCGTGCGGAGCATGAACAGGAATACATCAGGCGACAG CACCGCGTGGAGATGCCACGCCAGAACTCAGATCCCACCTCGGAAAATCCTCCTCCTCCCACTCGCATTGAAAA CCAGCATTAGCCAGAAAGAATTCTCCTGGGAATGGTAGTGCTCTGGGACCCAGACTAGGATCTCAACCCATCAGA atgecgagcgactcccggctcgaagcctggatgaataaatctctcggctctgagggaccctgcagggatctt CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT TTAGAGGAGGAGCAGAGACAGTTAGAGATCTTGCAGCAGCAGCTACTGCATGAACAAGCTCTACTTCTGGAATAT GTTTCCCTTCAGCATCAGCGGCAGGAGCAGAGGCCTGTGGAGAAGAAGAAGTGTACCATTACAAAGAAGGAATG **AGTCCTAGTGAGAAGCCAGCATGGGCCAAGGAGATCCCACATCTGGTAGCTGTAAAATCCCAGGGACCTGCCTTG** ACCGCCTCCCAGTCAGTGCACGAGCAGCCCACAAAGGGCCTCTCTGGGTTTCAGGAGGCTCTGAACGTGACCTCC TTTGACCGAAGCTCTTGGTTACGACAGGAAGAAGACATTCCACCAAAGGTGCCTCAAAGAACAACTTCTATATCC GCAAGCAACCCTGATCTCCGGAGAACTGAGCCCATCTTGGAGAGCCCCTTGCAGAGGACCAGCAGTGGCAGTTCC

FIG._27A



GAACGCACCAGAGTTCGAGCCAACAGTAAGTCAGAAGGATCACCTGTGCTTCCCCATGAGCCTGCCAAGGTGAAA CCAGAAGAATCCAGGGACATTACCCGGCCCAGTCGACCAGCTGATCTGACGGCATTAGCCAAAGAACTAAGAGAA AGCGAGGAAGAGGAAGATGGAGAGAGCGAGACCCATGATGGGACAGTGGCTGTCAGCGACATACCCAGACTG CATGCGGACAGTTTCAGCGGCAGTATTTCAAGAGAAGGAACCTTGATGATTAGAGAGACGTCTGGAGAGAAGAAG **ATCAGAAAATACAAGAAACGATTCAACTCAGAAATACTTTGTGCAGCTCTGTGGGGGTGTAAACCTTCTGGTGGGG** TCCAGCTCCAGCACCCCTAGCTCCCAGCCCAGCTCCCAAGGAGGCTCCCAGCCTGGATCACAAGCAGGATCCAGT CTCCGGATTGAAGAAACAAACCGCCCAATGAAGAAGGTGACTGATTACTCCTCCTCCAGTGAGGAGTCAGAAAGT ATACCAACAGGAGCTCCAGGCAGCAACGAGCAGTACAATGTGGGAATGGTGGGGACGCATGGGCTGGAGACCTCT CGATCTGGCCACAGTGACAGCAATGGCTTTGCTGGCCACATCAACCTCCCTGACCTGGTGCAGCAGAGCCATTCT CCAGCTGGAACCCCGACTGAGGGACTGGGGCGCGTCTCAACCCATTCCCAGGAGATGGACTCTGGGACTGAATAT GGCATGGGGAGCAGCACCAAAGCCTCCTTCACCCCCTTTGTGGACCCCCAGAGTATACCAGACGTCTCCCACTGAT GAAGATGAAGAGGATGAGGAATCATCAGCCGCAGCTCTGTTTACTAGCGAACTTCTTAGGCAAGAACAGGCCAAA CAGCAGATGGATGTGCTAGAGGGACTGAATGTCCTTGTGACAATTTCAGGAAAGAAGAATAAGCTACGAGTTTAC GGGGACTTGGAAGGCTGTATACATTATAAGTTGTTAAATATGAAAGGATCAAATTTTTGGTGATTGCCTTAAAG ACTCCTCATGCTATTGTCATCTTGCCTAAAACAGATGGAATGGAAATGCTTGTTTGCTATGAGGATGAGGGGGGTG actgaaaatggcctgatgcttttggaccgaagtgggcaaggcaaagtctataatctgatcaaccggaggcgattt <u> AATGCTGTGGAAATATATGCTTGGGCTCCTAAACCGTATCATAAATTCATGGCATTTAAGTCTTTTGCAGATCTC</u> CAGCACAAGCCTCTGCTAGTTGATCTCACGGTAGAAGAAGGTCAAAGATTAAAGGTTATTTTTGGTTCACACACT GGTTTCCATGTAATTGATGTTGATTCAGGAAACTCTTATGATATCTACATACCATCTCATATTCAGGGCAATATC TATGTAAACACCTATGGCCGGATAACTAAGGATGTGGTGCTCCAATGGGGAGAAATGCCCACGTCTGTGGCCTAC ATTCATTCCAATCAGATAATGGGCTGGGGCGAGAAAGCTATTGAGATCCGGTCAGTGGAAACAGGACATTTGGAT GTGCGATCTGGAGGAAGTAGCCAAGTGTTTTTCATGACCCTCAACAGAAATTCCATGATGAACTGGTAA

FIG._27B



CCTCGGCTGAAGTCTAAGAAGTGGTCAAAAAATTCCAGTCATTTATTGAGAGCTGCTTGGTAAAGAATCACAGC AGTGAGGAAGAAGAGGAGAATGACTCAGGAGAGCCCCAGCTCCATCCTGAATCTGCCAGGGGAGTCGACGCTG CGGAGGGACTTTCTGAGGCTGCAGCTGGCCAACAAGGAGCGTTCTGAGGCCCTACGGAGGCAGCAGCTGGAGCAG CAGCAGCGGGAGAATGAGGAGCACAAGCGGCAGCTGCTGGCCGAGCGTCAGAAGCGCATCGAGGAGCAGAAAGAG CAGAGGCGGCGGCTGGAGGAGCAACAAAGGCGAGAAGGAGCTGCGGAAGCAGCAGCAGGAGGAGCAGCCGG CATCAGCGGCAGGAGCAGAGGCCTGTGGAGAAGAAGCCACTGTACCATTACAAAGAAGGAATGAGTCCTAGTGAG AAGCCAGCATGGGCCAAGGAGATCCCACATCTGGTAGCTGTAAAATCCCAGGGACCTGCCTTGACCGCCTCCCAG reagtecaceaceceacapaagegeetetetegettteaggagetetegagetetegagetetegagetegag **ATGGCGAGCGACTCCCCGGCTCGAAGCCTGGATGAATAGATCTCTCGGCTCTGAGGGACCCTGCAGGGATCTTT** GCAGCCATCAAGGTTATGGATGTCACAGGGGATGAAGAGGAAGAAATCAAACAAGAAATTAACATGTTGAAGAAA CTTTGGTTGGTGATGGAGTTTTGTGGTGCTGCTCTGTCACCGACCTGATCAAGAACACAAAAGGTAACACGTTG AAAGAGGAGTGGATTGCATACATCTGCAGGGAAATCTTACGGGGGCTGAGTCACCTGCACCAGCATAAAGTGATT CATCGAGATATTAAAGGGCAAAATGTCTTGCTGACTGAAATGCAGAAGTTAAACTAGTGGACTTTGGAGTCAGT GCTCAGCTTGATCGAACAGTGGGCAGGAGGAATACTTTCATTGGAACTCCCTACTGGATGGCACCAGAAGTTATT GCCTGTGATGAAAACCCAGATGCCACATATGATTTCAAGAGTGACTTGTGGGTCTTTGGGTATCACCGCCATTGAA ATGGCAGAGGAGCTCCCCCTCTCTGTGACATGCACCCCATGAGAGCTCTCTTCCTCATCCCCCGGAATCCAGCG CAGCGACCAGCAACAGAACAATTGATGAAGCATCCATTTATACGAGACCAACCTAATGAGCGACAGGTCCGCATT CACTATGAGGAGCAGATGCGCCGGGAGGAGGAGGAGGAGGCGTGCGGAGCATGAACAGGAATATAAGCGCAAACAA ATGCCACGCCAGAACTCCAGATCCCACCTCGGAAATCCTCCTCCCCACTCGCATTGAAAAGTTTGACCGAAGC **PCTTGGTTACGACAGGAAGAGACATTCCACCAAAGGTGCCTCAAAGAACAACTTCTATATCCCCAGCATTAGCC** GATCTCCGGAGAGCTGAGCCCATCTTGGAGGCCCCTTGCAGAGGACCAGCAGTGGCAGTTCCTCCAGCTCCAGC ACCCCTAGCTCCCAGCCCAGCTCCCAAGGAGGCTCCCAGCCTGGATCACAAGCAGGATCCAGTGAACGCACAGA GAATTGGTGGAACTTGTTGGAAATGGAACATACGGGCAAGTTTATAAGGGTCGTCATGTCAAAACGGGCCAGCTT



GAAACAAACCGCCCAATGAAGAAGGTGACTGATTACTCCTCCTCCAGTGAGGAGTCAGAAAGTAGCGAGGAAGAG GTTCGAGCCAACAGTAAGTCAGAAGGATCACCTGTGCTTCCCCATGAGCCTGCCAAGGTGAAAACCAGAAGAATCC GCTCCAGGCAGCAACGAGCAGTACAATGTGGGAATGGTGGGGACGCATGGGCTGGAGACCTCTCTCATGCGGACAG ITCAGCGGCAGTATTTCAAGAAGGAACCTTGATGATTAGAGAGACGTCTGGAGAGAAGAAGAAGGATCTGGCCAC <u> AGTGACAGCAATGGCTTTTGCTGGCCACATCAACCTCCCTGACCTGGTGCAGCAGAGCCATTCTCCAGCTGGAACC</u> CCGACTGAGGGACTGGGGGGGGGGTCTCAACCCATTCCCAGGAGATGGACTTGGGACTGAATATGGCATGGGGAGC **AGCACCAAAGCCTCCTTCACCCCCTTTGTGGACCCCAGAGTATACCAGACGTCTCCCACTGATGAAGATGAAGAG** GATGAGGAATCATCAGCCGCAGCTCTGTTTACTAGCGAACTTCTTAGGCAAGAACAGGCCAAACTCAATGAAGCA **AAGAAACGATTCAACTCAGAAATACTTTGTGCAGCTCTGTGGGGTGTAAACCTTCTGGTGGGGACTGAAAATGGC** GTGCTAGAGGGACTGAATGTCCTTGTGACAATTTCAGGAAAGAAGAATAAGCTACGAGTTTACTATCTTTCATGG TTAAGAAACAGAATACTACATAATGACCCAGAAGTAGAAAAGAAACAAGGCTGGATCACTGTTGGGGACTTGGAA GGCTGTATACATTATAAAGTTGTTAAATATGAAAGGATCAAATTTTTGGTGATTGCCTTAAAGAATGCTGTGGAA CTGCTAGTTGATCTCACGGTAGAAGAAGGTCAAAGATTAAAGGTTATTTTTGGTTCACACACTGGTTTCCATGTA AGGGACATTACCCGGCCCAGTCGACCAGCTGATCTGACGGCATTAGCCAAAGAACTAAGAGAACTCCGGATTGAA GAGGAAGATGGAGAGAGCGAGACCCATGATGGGACAGTGGCTGTCAGCGACATACCCAGACTGATACCAACAGGA CTGATGCTTTTGGACCGAAGTGGGCAAGGCAAAGTCTATAATCTGATCAACCGGAGGCGATTTCAGCAGATGGAT **ATATATGCTTGGGCTCCTAAACCGTATCATAATTCATGGCATTTAAGTCTTTTGCAGATCTCCAGCACAAGCCT** ATTGATGTTGATTCAGGAAACTCTTATGATATCTACATACCATCTCATATTCAGGGCAATATCACTCCTCATGCT GGAAGTAGCCAAGTGTTTTTCATGACCCTCAACAGAAATTCCATGATGAACTGGTAA

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MASDSPARSLDEIDLSALRDPAGIFELVELVGNGTYGQVYKGRHVKTGQLAAIKVMDVTG NKERS EALRROOL EOOORENE EHKROLLAEROKRI EEOKEORRREE EOORREKELRKOOE REORRHY EEQMRREE ERRRAEHE OEYKRKOLEE OROAERLOROLKOERDYLVSLOHOROE **ORPVEKKPLYHYKEGMSPSEKPAWAKEVEERSRLNROSSPAMPHKVANRISDPNLPPRSE** SHRVEMPRQNSDPTSENPPLPTRIEKFDRSSWLRQEEDIPPKVPQRTTSISPALARKNSP GNGSALGPRLGSQPIRASNPDLRRTEPILESPLQRTSSGSSSSSSTPSSQPSSQGGSQPG ELRELRIEETNRPMKKVTDYSSSSEESESESEEEEEDGESETHDGTVAVSDIPRLIPTGAP)EEEEIKOEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSVTDLIKNT KGNTLKEEWIAYICREILRGLSHLHQHKVIHRDIKGONVLLTENAEVKLVDFGVSAQLDR OLKDHIDRTKKKRGEKDETEYEYSGSEEEEENDSGEPSSILNLPGESTLRRDFLRLQLA SFSISGVQPARTPPMLRPVDPQIPHLVAVKSQGPALTASQSVHEQPTKGLSGFQEALNVT SQAGSSERTRVRANSKSEGSPVLPHEPAKVKPEESRDITRPSRPASYKKAIDEDLTALAK GSNEQYNVGMVGTHGLETSHADSFSGSISREGTLMIRETSGEKKRSGHSDSNGFAGHINL PDLVQQSHSPAGTPTEGLGRVSTHSQEMDSGTEYGMGSSTKASFTPFVDPRVYQTSPTDE **DEEDEESSAAALFTSELLRQEQAKLNEARKISVVNVNPTNIRPHSDTPEIRKYKKRFNSE** 1261 HSNQIMGWGEKAIEIRSVETGHLDGVFMHKRAQRLKFLCERNDKVFFASVRSGGSSQVFF IVGRRNTFIGTPYWMAPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR ALFLI PRNPAPRLKSKKWSKKFQSFIESCLVKNHSQRPATEQLMKHPFIRDQPNERQVRI ILCAALWGVNLLVGTENGLMLLDRSGQGKVYNL INRRRFQQMDVLEGLNVLVTISGKKNK LRVYYLSWLRNRILHNDPEVEKKQGWITVGDLEGCIHYKVVKYERIKFLVIALKNAVEIY AWAPKPYHKFMAFKSFADLQHKPLLVDLTVEEGQRLKVIFGSHTGFHVIDVDSGNSYDIY IPSHIQGNITPHAIVILPKTDGMEMLVCYEDEGVYVNTYGRITKDVVLQWGEMPTSVAYI MTLNRNSMMNWZ 1021 241 301 361 421 481 541 601 661 721 781 841 901 961 181

FIG._29



MASDSPARSLDEIDLSALRDPAGIFELVELVGNGTYGQVYKGRHVKTGQLAAIKVMDVTG

DEEEEIKQEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSVTDLIKNT

181 241 301 361 421 481 541 601 661 721 781 841 901 961

QLKDHIDRTKKKRGEKDETEYEYSGSEEEEENDSGEPSSILNLPGESTLRRDFLRLQLA NKERSEALRRQQLEQQQRENEEHKRQLLAERQKRIEEQKEQRRRLEEQQRREKELRKQQE REQRRHYEEQMRREEERRRAEHEQEYIRRQLEEEQRQLEILQQQLLHEQALLLEYKRKQL FDRSSWLRQEEDI PPKVPQRTTS ISPALARKNS PGNGSALGPRLGSQP I RASNPDLRRTE PILESPLORTSSGSSSSSSTPSSOPSSOGGSOPGSOAGSSERTRVRANSKSEGSPVLPHE SESSEEEEEDGESETHDGTVAVSDIPRLIPTGAPGSNEQYNVGMVGTHGLETSHADSFSG EARKISVVNVNPTNIRPHSDTPEIRKYKKRFNSEILCAALWGVNLLVGTENGLMLLDRSG KGNTLKEEWIAYICREILRGLSHLHQHKVIHRDIKGQNVLLTENAEVKLVDFGVSAQLDR IVGRRNTFIGTPYWMAPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR ALFLIPRNPAPRLKSKKWSKKFQSFIESCLVKNHSQRPATEQLMKHPFIRDQPNERQVRI EEQRQAERLQRQLKQERDYLVSLQHQRQEQRPVEKKPLYHYKEGMSPSEKPAWAKEIPHL VAVKSQGPALTASQSVHEQPTKGLSGFQEALNVTSHRVEMPRQNSDPTSENPPLPTRIEK PAKVKPEESRDITRPSRPASYKKAIDEDLTALAKELRELRIEETNRPMKKVTDYSSSSEE SISREGTLMIRETSGEKKRSGHSDSNGFAGHINLPDLVQQSHSPAGTPTEGLGRVSTHSQ EMDSGTEYGMGSSTKASFTPFVDPRVYQTSPTDEDEEDEESSAALFTSELLRQEQAKLIN QGKVYNLINRRRFQQMDVLEGLNVLVTISGKKNKLRVYYLSWLRNRILHNDPEVEKKQGW DLTVEEGORLKVIFGSHTGFHVIDVDSGNSYDIYIPSHIQGNITPHAIVILPKTDGMEML 1201 VCYEDEGVYVNTYGRITKDVVLQWGEMPTSVAYIHSNQIMGWGEKAIEIRSVETGHLDGV ITVGDLEGCIHYKVVKYERIKFLVIALKNAVEIYAWAPKPYHKFMAFKSFADLQHKPLLV FMHKRAQRLKFLCERNDKVFFASVRSGGSSQVFFMTLNRNSMMWZ 1021

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MASDSPARSLDEIDLSALRDPAGIFELVELVGNGTYGQVYKGRHVKTGOLAAIKVMDVTG)EEEEIKOEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSVTDLIKNT KGNTLKEEWIAYICREILRGLSHLHQHKVIHRDIKGQNVLLTENAEVKLVDFGVSAQLDR TYGRRNTFIGTPYWMAPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR OLKDHIDRTKKKRGEKDETEYEYSGSEEEEEENDSGEPSSILNLPGESTLRRDFLRLQLA NKERSEALRRQQLEQQQRENEEHKRQLLAERQKRIEEQKEQRRRLEEQQRREKELRKQQE REORRHYEEQMRREEERRRAEHEQEYIRROLEEEQROLEILQQQLLHEQALLLEYKRKOL **EEQRQAERLQRQLKQERDYLVSLQHQRQEQRPVEKKPLYHYKEGMSPSEKPAWAKEVEER** SRLNRQSSPAMPHKVANRISDPNLPPRSESFSISGVQPARTPPMLRPVDPQIPHLVAVKS **QGPALTASQSVHEQPTKGLSGFQEALNVTSHRVEMPRQNSDPTSENPPLPTRIEKFDRSS** WLRQEEDIPPKVPQRTTSISPALARKNSPGNGSALGPRLGSQPIRASNPDLRRTEPILES PLORTSSGSSSSSSTPSSQPSSQGGSQPGSQAGSSERTRVRANSKSEGSPVLPHEPAKVK PEESRDITRPSRPADLTALAKELRELRIEETNRPMKKVTDYSSSSEESESEEEEDGES ETHDGTVAVSDIPRLIPTGAPGSNEQYNVGMVGTHGLETSHADSFSGSISREGTLMIRET SGEKKRSGHSDSNGFAGHINLPDLVQQSHSPAGTPTEGLGRVSTHSQEMDSGTEYGMGSS TKASFTPFVDPRVYQTSPTDEDEEDEESSAAALFTSELLRQEQAKLNEARKISVVNVNPT NIRPHSDTPEIRKYKKRFNSEILCAALWGVNLLVGTENGLMLLDRSGQGKVYNLINRRRF QQMDVLEGLNVLVTI SGKKNKLRVYYLSWLRNR I LHNDPEVEKKQGWITVGDLEGCIHYK **VVKYERIKFLVIALKNAVEIYAWAPKPYHKFMAFKSFADLQHKPLLVDLTVEEGORLKVI** FGSHTGFHVIDVDSGNSYDIYIPSHIQGNITPHAIVILPKTDGMEMLVCYEDEGVYVNTY GRITKDVVLQWGEMPTSVAYIHSNQIMGWGEKAIEIRSVETGHLDGVFMHKRAQRLKFLC ALFLI PRNPAPRLKSKKWSKKFQSFIESCLVKNHSQRPATEQLMKHPFIRDQPNERQVRI ERNDKVFFASVRSGGSSQVFFMTLNRNSMMWZ 1801 1021 421 721 781 841 901 196 181 241 301 361 481 541 601 661

FIG._31



OLKDHIDRTKKKRGEKDETEYEYSGSEEEEENDSGEPSSILNLPGESTLRRDFLRLQLA RKNSPGNGSALGPRLGSQPIRASNPDLRRTEPILESPLQRTSSGSSSSSTPSSQPSSQG MASDSPARSLDEIDLSALRDPAGIFELVELVGNGTYGQVYKGRHVKTGOLAAIKVMDVTG NKERSEALRROOLEOOORENEEHKROLLAEROKRIEEOKEORRLEEOORREKELRKOOE REQRRHYEEQMRREEERRRAEHEQEYKRKQLEEQRQAERLQRQLKQERDYLVSLQHQRQE **ORPVEKKPLYHYKEGMSPSEKPAWAKEIPHLVAVKSQGPALTASQSVHEQPTKGLSGFQE** GSOPGSOAGSSERTRVRANSKSEGSPVLPHEPAKVKPEESRDITRPSRPASYKKAIDEDL PTGAPGSNEQYNVGMVGTHGLETSHADSFSGSISREGTLMIRETSGEKKRSGHSDSNGFA SYDIYIPSHIOGNITPHAIVILPKTDGMEMLVCYEDEGVYVNTYGRITKDVVLOWGEMPT SVAYIHSNQIMGWGEKAIEIRSVETGHLDGVFMHKRAQRLKFLCERNDKVFFASVRSGGS KGNTLKEEWIAYICREILRGLSHLHQHKVIHRDIKGQNVLLTENAEVKLVDFGVSAQLDR IVGRRNTFIGTPYWMAPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR ALFLI PRNPAPRLKSKKWSKKFQSFIESCLVKNHSQRPATEQLMKHPFIRDQPNERQVRI alinvitshrvempronsdpitsenpplptriekfdrsswlroeedippkvportisispala TALAKELRELRIEETNRPMKKVTDYSSSSEESESESEEEEDGESETHDGTVAVSDIPRLI SPTDEDEEDEESSAAALFTSELLRQEQAKLNEARKISVVNVNPTNIRPHSDTPEIRKYKK RFNSEILCAALWGVNLLVGTENGLMLLDRSGQGKVYNLINRRRFQQMDVLEGLNVLVTIS GKKNKLRVYYLSWLRNRILHNDPEVEKKQGWITVGDLEGCIHYKVVKYERIKFLVIALKN AVEIYAWAPKPYHKFWAFKSFADLQHKPLLVDLTVEEGQRLKVIFGSHTGFHVIDVDSGN DEEEEIKQEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSVTDLIKNT **3HINLPDLVQQSHSPAGTPTEGLGRVSTHSQEMDSGTEYGMGSSTKASFTPFVDPRVYQT** SQVFFMTLNRNSMMNWZ 1021 181 241 301 361 421 481 541 199 781 841 901 196 601 721



MASDSPARSLDEIDLSALRDPAGIFELVELVGNGTYGQVYKGRHVKTGQLAAIKVMDVTG **QLKDHIDRTKKKRGEKDETEYEYSGSEEEEENDSGEPSSILNLPGESTLRRDFLRLQLA** nkersealrrooleoooreneehkrollaerokrieeokeorrrleeoorrekelrkooe REQRRHYEEQMRREEERRRAEHEQEYKRKQLEEQRQAERLQRQLKQERDYLVSLQHQRQE **2RPVEKKPLYHYKEGMSPSEKPAWAKEVEERSRLNRQSSPAMPHKVANRISDPNLPPRSE** SFSISGVQPARTPPMLRPVDPQIPHLVAVKSQGPALTASQSVHEQPTKGLSGFQEALNVT SHRVEMPRQNSDPTSENPPLPTRIEKFDRSSWLRQEEDIPPKVPQRTTSISPALARKNSP GNGSALGPRLGSQPIRASNPDLRRTEPILESPLQRTSSGSSSSSSTPSSQPSSQGGSQPG SOAGSSERTRVRANSKSEGSPVLPHEPAKVKPEESRDITRPSRPADLTALAKELRELRIE GMVGTHGLETSHADSFSGSISREGTLMIRETSGEKKRSGHSDSNGFAGHINLPDLVQQSH SPAGTPTEGLGRVSTHSQEMDSGTEYGMGSSTKASFTPFVDPRVYQTSPTDEDEEDS **AAALFTSELLRQEQAKLNEARKISVVNVNPTNIRPHSDTPEIRKYKKRFNSEILCAALWG** VNLLVGTENGLMLLDRSGQGKVYNLINRRRFQQMDVLEGLNVLVTISGKKNKLRVYYLSW KGNTLKEEWIAYICREILRGLSHLHQHKVIHRDIKGQNVLLTENAEVKLVDFGVSAQLDR IVGRRNTFIGTPYWMAPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR ALFLIPRNPAPRLKSKKWSKKFQSFIESCLVKNHSQRPATEQLMKHPFIRDQPNERQVRI ETNR PMKKVTDYSSSSEESESSEEEEEDGESETHDGTVAVSDI PRLI PTGAPGSNEQYNV LRNRILHNDPEVEKKQGWITVGDLEGCIHYKVVKYERIKFLVIALKNAVEIYAWAPKPYH KFMAFKSFADLQHKPLLVDLTVEEGQRLKVI FGSHTGFHVIDVDSGNSYDIYI PSHIQGN ITPHAIVILPKTDGMEMLVCYEDEGVYVNTYGRITKDVVLQWGEMPTSVAYIHSNQIMGW GEKAIEIRSVETGHLDGVFMHKRAQRLKFLCERNDKVFFASVRSGGSSQVFFMTLNRNSM DEEEEIKQEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSVTDLIKNT 081 141 201 1021 181 241 301 361 421 541 601 661 781 841 901 196 121 481 721

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MASDSPARSLDEIDLSALRDPAGIFELVELVGNGTYGQVYKGRHVKTGQLAAIKVMDVTG NRRRFQQMDVLEGLNVLVTISGKKNKLRVYYLSWLRNRILHNDPEVEKKQGWITVGDLEG CIHYKVVKYERIKFLVIALKNAVEIYAWAPKPYHKFMAFKSFADLQHKPLLVDLTVEEGQ DEEEEIKQEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSVTDLIKNT KGNTLKEEWIAYICREILRGLSHLHQHKVIHRDIKGQNVLLTENAEVKLVDFGVSAQLDR IVGRRNTFIGTPYWMAPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR ALFLI PRNPAPRLKSKKWSKKFQSFIESCLVKNHSQRPATEQLMKHPFIRDQPNERQVRI **JLKDHIDRTKKKRGEKDETEYEYSGSEEEEEENDSGEPSSILNLPGESTLRRDFLRLQLA** NKERS EALRROOL EOQORENE EHKROLLAEROKR I EEOKEORRRLE EOORREKELRKOOE REORRHYEEOMRREEERRRAEHEQEYIRROLEEEQROLEILOQOOLLHEQALLLEYKRKOL EEQRQAERLQRQLKQERDYLVSLQHQRQEQRPVEKKPLYHYKEGMSPSEKPAWAKEIPHL VAVKSQGPALTASQSVHEQPTKGLSGFQEALNVTSHRVEMPRQNSDPTSENPPLPTRIEK FDRSSWLRQEEDI PPKVPQRTTS I SPALARKNS PGNGSALGPRLGSQP I RASNPDLRRTE PILESPLORTSSGSSSSSTPSSOPSSOGGSOPGSOAGSSERTRVRANSKSEGSPVLPHE PAKVKPEESRDITRPSRPADLTALAKELRELRIEETNRPMKKVTDYSSSSEESESEEE EDGESETHDGTVAVSDI PRLI PTGAPGSNEQYNVGMVGTHGLETSHADS FSGS I SREGTL MIRETSGEKKRSGHSDSNGFAGHINLPDLVQQSHSPAGTPTEGLGRVSTHSQEMDSGTEY GMGSSTKASFTPFVDPRVYQTSPTDEDEEDEESSAAALFTSELLRQEQAKLNEARKISVV NVNPTNIRPHSDTPEIRKYKKRFNSEILCAALWGVNLLVGTENGLMLLDRSGQGKVYNLI RLKVI FGSHTGFHVIDVDSGNSYDIYIPSHIQGNITPHAIVILPKTDGMEMLVCYEDEGV YVNTYGRITKDVVLQWGEMPTSVAYIHSNQIMGWGEKAIEIRSVETGHLDGVFMHKRAQR LKFLCERNDKVFFASVRSGGSSQVFFMTLNRNSMMWZ 1021 961 721 781 841 901 121 181 241 301 361 421 481 541 601 661

FIG._34



MASDS PARSLDEI DLSALRDPAGI FELVELVGNGTYGQVYKGRHVKTGQLAAI KVMDVTG REQRRHY EEQMRREEERRRAEHEQEYKRKQLEEQRQAERLQRQLKQERDYLVSLQHQRQE **QRPVEKKPLYHYKEGMSPSEKPAWAKEIPHLVAVKSQGPALTASQSVHEQPTKGLSGFQE** RKNSPGNGSALGPRLGSQPIRASNPDLRRTEPILESPLQRTSSGSSSSSSTPSSQPSSQG)EEEEIKQEINMLKKYSHHRNIATYYGAFIKKNPPGMDDQLWLVMEFCGAGSVTDLIKNT KGNTLKEEWIAYICREILRGLSHLHQHKVIHRDIKGQNVLLTENAEVKLVDFGVSAQLDR TVGRRNTFIGTPYWMAPEVIACDENPDATYDFKSDLWSLGITAIEMAEGAPPLCDMHPMR NKERS EALRROOL EOOORENE EHKROLLAEROKRIEEOKEORRRLEEOORREKELRKOOE ALNVTSHRVEMPRQNSDPTSENPPLPTRIEKFDRSSWLRQEEDIPPKVPQRTTSISPALA GSQPGSQAGSSERTRVRANSKSEGSPVLPHEPAKVKPEESRDITRPSRPADLTALAKELR ALFLI PRNPAPRLKSKKWSKKFOSFIESCLVKNHSQRPATEQLMKHPFIRDQPNERQVRI OLKDHIDRTKKKRGEKDETEYEYSGSEEEEEENDSGEPSSILNLPGESTLRRDFLRLOLA ELRIEETNRPMKKVTDYSSSSEESESSEEEEEDGESETHDGTVAVSDIPRLIPTGAPGSN EQYNVGMVGTHGLETSHADSFSGSISREGTLMIRETSGEKKRSGHSDSNGFAGHINLPDL VQQSHSPAGTPTEGLGRVSTHSQEMDSGTEYGMGSSTKASFTPFVDPRVYQTSPTDEDEE **DEESSAAALFTSELLRQEQAKLNEARKISVVNVNPTNIRPHSDTPEIRKYKKRFNSEILC AALWGVNLLVGTENGLMLLDRSGQGKVYNLINRRRFQQMDVLEGLNVLVTISGKKNKLRV** YYLSWLRNRILHNDPEVEKKQGWITVGDLEGCIHYKVVKYERIKFLVIALKNAVEIYAWA PKPYHKFMAFKSFADLQHKPLLVDLTVEEGQRLKVIFGSHTGFHVIDVDSGNSYDIYIPS 1141 HIQGNITPHAIVILPKTDGMEMLVCYEDEGVYVNTYGRITKDVVLQWGEMPTSVAYIHSN QIMGWGEKAIEIRSVETGHLDGVFMHKRAQRLKFLCERNDKVFFASVRSGGSSQVFFMTL 1021 1201 196 181 241 301 361 421 481 541 601 199 721 781 841 901

FIG._35